

REMARKS

I. Introduction:

Claims 10 and 11 are amended herein. Claims 38-41 have been withdrawn from consideration by the Examiner as being directed to a non-elected distinct invention. Claims 1-37 and 42-53 are currently pending.

II. Specification:

The abstract has been amended as requested by the Examiner. More specifically, the term 'disclosed' has been removed.

III. Claim Rejections Under 35 U.S.C. §112:

Claims 10 and 11 have been amended to replace 'base member' with 'base'. As amended, claims 10-12 are believed to comply with 35 U.S.C. §112.

IV. Claim Rejections Under 35 U.S.C. §102(b):

Claims 1, 2, 10, 17-19, 21-25, 29, 31, 33-35, 37, 42-47, 49, and 51-53 stand rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 5,324,483 (Cody et al.).

Claim 1 generally requires a base having a plurality of reaction wells formed therein, a cover configured for sealing engagement with the base to form a housing and define a common pressure chamber in communication with the reaction wells, and an inlet port in communication with the pressure chamber for supplying pressurized fluid to the chamber to pressurize the reaction wells. Each of the reaction wells has a closed lower end and an open upper end for receiving components for a reaction. The housing is configured to sustain a pressure substantially above atmospheric pressure.

Applicants respectfully submit that the apparatus as set forth in claim 1 is not anticipated by Cody et al., which disclose an apparatus for solid phase synthesis. The apparatus includes a reservoir block 15 having a plurality of wells 16, a plurality of reaction tubes 11 with filters 14 on their lower ends, a holder block 18 having a plurality of apertures 19, and a manifold 20 which may include ports 23 to allow introduction or maintenance of a controlled environment (see Figs. 1 and 3). The Cody et al. patent is directed to solid phase synthesis which focuses on chemical reactions of substrates attached to solid supports (e.g., polystyrene, polyethylene glycol, cellulose, controlled-pore glass), including methods for attachment and detachment from the supports. [See, for example, col. 2, lines 56-68, col. 3, lines 4-6 (“The approach described herein greatly increases the flexibility and diversity of structures that can be produced by a parallel, solid phase synthesis technology.”), col. 3, lines 10-15 (“The key feature [] provides a unique means to segregate and manipulate the growing compounds on a solid support.”).] Overall, there is no teaching in Cody et al. that covers pressurization substantially above atmospheric pressure. Since solid phase synthesis applications of small organic molecules typically do not use a pressurized reacting gas.

As noted by the Examiner, the reaction wells of the Cody et al. apparatus are constructed of a material which is capable of withstanding reactive components and manipulations. The Cody et al. patent specifies that the manifold provides an air-tight chamber which facilitates manipulation common to solid phase organic synthesis (col. 9, lines 25-36 (“...The ports (23) allow control over atmosphere within the manifold (20) and provide a means to sparge the reaction tubes (11).”)). Gasket 24 is placed between the holder block 18 and manifold 20 to create a sealing effect between the manifold and the holder block to allow manipulations and inert atmosphere (col. 9, lines 46-50). The apparatus of Cody et al. is thus pressurized in the context of manipulation (i.e., forcing liquid contents of reaction wells through a filter plate) and not reaction. Such manipulation requires only nominal pressure or

an inert atmosphere. Hence, Cody et al. do not disclose an apparatus configured for pressurization substantially above atmospheric pressure.

As further evidence that the apparatus of Cody et al. is not designed to withstand pressure substantially above atmospheric pressure, a preferred embodiment utilizes a piercable septum (gasket) 34 to seal the chamber (Figs. 1 and 6). The gasket 34 may be made from a rubber that is puncturable with a needle-like object and reseals following the puncture (col. 10, lines 7-12). Once the septum is pierced, the chamber will not be able to sustain significant pressures (e.g., above about 1 or 2 psig).

Thus, the apparatus of Cody et al. is configured to sustain only an inert atmosphere or nominal pressures for use in physical manipulation for solid phase synthesis, as is well understood by those skilled in the art. In contrast, applicants' apparatus is designed to sustain an operating pressure substantially above atmospheric pressure and can be used, for example, for gas phase polymerization or other gas phase reactions.

Furthermore, the base of Cody et al. does not include reaction wells formed in an upper surface of the base and extending partially therethrough, with the reaction wells having a closed lower end defined by the base, as required by claim 1. The closed lower ends of the reaction wells formed by the base in applicants' apparatus provide for a simple, cost effective design which allows for pressurization of the reaction wells with a pressurized gas at a pressure substantially above atmospheric pressure. Since sealing is required only for the common pressure chamber, the apparatus provides increased reliability and simplified maintenance. In contrast, the reservoir block 15 of Cody et al. consists of a reservoir rack 41 which is adapted to hold removable reaction wells 16 (Fig. 5). Without the reaction wells 16 inserted into the base, there is no reaction well formed for holding reaction components.

Accordingly, claim 1 is submitted as patentable over Cody et al. and the other prior art of record.

Claims 2-30, depending either directly or indirectly from claim 1, are submitted as patentable for the reasons discussed above with respect to claim 1.

Claims 17-25 are further submitted as not anticipated by Cody et al. which do not show a flow restriction device positioned adjacent to open ends of reaction wells to provide communication between the reaction wells and pressure chamber while reducing cross-talk between the reaction wells.

The Examiner identifies gasket 26 of the Cody et al. apparatus as a flow restriction device. Gasket 26 is interposed between the reservoir block 15 and the holder block 18 (Figs. 2, 3, and 5). The gasket 26 does not provide communication between the reaction wells and a sealed chamber (i.e., chamber formed by manifold 20). As shown in Fig. 5 and described at col. 9, lines 46-47, gaskets 24 and 26 are used to seal the reaction wells from the chamber. Gasket 26 also seals open ends of the reaction wells 16 from one another.

Moreover, there are no vent holes or micromachined flow restrictions formed in the gasket, as specified by claims 18 and 19.

Claim 31 is directed to an apparatus for use in parallel synthesis of screening materials and generally includes a pressure chamber sized for receiving a microtiter plate, where the microtiter plate has reaction wells with a closed lower end and an open upper end exposed to the pressure chamber, a cover movable between an open and closed position, an inlet port in communication with the pressure chamber for supplying fluid pressurized substantially above atmospheric pressure to the pressure chamber, and a quick-operating fastening device operable to position the cover in its closed position and hold the cover in sealing engagement with the pressure chamber.

The apparatus set forth in claim 31 is not anticipated by Cody et al., which do not show a pressure chamber sized for receiving a microtiter plate. The chamber of

Cody et al. is formed by manifold 20 and holder block 18 and is configured for receiving reaction tubes 11 (Fig. 4). Furthermore, as previously discussed, the apparatus of Cody et al. does not provide a pressure chamber for receiving fluid pressurized substantially above atmospheric pressure.

Accordingly, claim 31 is submitted as patentable over Cody et al. and the other prior art of record.

Claims 32-37, depending either directly or indirectly from claim 31, are submitted as patentable for the same reasons as claim 31.

Claims 33, 34, 35, and 37 are further submitted as patentable for the reasons discussed above with respect to claims 17, 18, 19 and 25, respectively.

Claim 42 is directed to an apparatus for use in parallel reaction of materials and generally includes a base having a plurality of reaction wells with closed lower ends and open upper ends, a cover configured for sealing engagement with the base to form a housing defining a common pressure chamber in communication with the reaction wells, a flow restriction device positioned adjacent top the open ends of the reaction wells to provide communication between the reaction wells and pressure chamber while reducing cross-talk between the reaction wells, and an inlet port in communication with the pressure chamber. Claim 42 is submitted as patentable for the reasons discussed above with respect to claim 17.

Claims 43-51, depending either directly or indirectly from claim 42, are submitted as patentable for the same reasons as claim 42.

Claims 46 and 47 are further submitted as patentable for the reasons discussed above with respect to claims 18 and 19, respectively.

Claim 52 is directed to an apparatus for use in parallel reaction of materials and generally requires a base having a plurality of reaction wells formed therein, a cover configured for sealing engagement with the base to form a housing and define a common pressure chamber in communication with the reaction wells, and an inlet

port in communication with the pressure chamber for supplying pressurized fluid to the chamber to pressurize the reaction wells. Each of the reaction wells has a permanently closed lower end and an open upper end for receiving components for a reaction. The housing is configured to sustain a pressure above 40 psig.

As previously discussed with respect to claim 1, the apparatus of Cody et al. is not designed to operate at pressures substantially above atmospheric pressure and does not disclose sustaining pressures above 40 psig.

Accordingly, claim 52 is submitted as nonobvious and patentable over Cody et al. and the other prior art of record.

Claim 53, depending directly from claim 52, is submitted as patentable for the same reasons as claim 52.

V. Claim Rejections Under 35 U.S.C. §103(a):

Claims 2-4, 52, and 53 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Cody et al. in view of U.S. Patent No. 5,428,118 (Painter et al.), "Investigation of Coolant Mixing in Pressurized Water Reactors at the Rossendorf Mixing Test Facility ROCOM" (Grunwald et al.), and "Runaway in Stirred Tanks" (Heiszwolf).

Claims 2-4, 52, and 53 all require, among other things, a housing configured to sustain an operating pressure of at least 10 psig.

Painter et al. disclose a gas phase fluidized bed polyolefin polymerization process using gas or gas-solid tangential flow. Tangential flow of gas is provided in an expanded section of the gas phase reactor to reduce fine entrainment into the gas cycle system and reduce solid particle build-up on interior surfaces of the expanded section of the reactor. A gas phase fluidized bed reactor 1 is used for the process (Fig. 1). A first portion of fluidizing gas is supplied through inlet 13 and a second

portion of the gas is supplied to the expanded section of the reactor via lines connecting to nozzle 6. A compressor 11 and heat exchanger 12 are included to provide gas at different phases to the reactor. The apparatus does not include individual reaction wells for parallel synthesis or screening and is not concerned with sealing individual reaction wells.

The disclosure of Cody et al. is generally limited to solid phase synthesis (see Col. 3, lines 1-3), whereas Painter et al. deal with gas phase polymerization. The apparatus of Cody et al. is designed to operate at low pressures (e.g., nominal pressure for physical manipulations or inert atmosphere) and would require significant modification for operation substantially above atmospheric pressure, not just with regard to the manifold material but also as to the sealing arrangement and simple spring clips used to hold the assembly together.

Heiszwolf discusses stability criteria for batch and continuous reactors. The reactor is enclosed by a Plexiglas box to prevent injury to lab personnel in the case of a reactor explosion. The Plexiglas box is not used to create a pressure chamber suitable for sustaining pressure during a reaction. The Grunwald et al. reference is directed to coolant mixing in pressurized water reactors and does not remedy the deficiencies of the primary reference.

Accordingly, claims 2-4, 52, and 53 are submitted as patentable over the prior art of record.

Claim 5 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Cody et al. in view of U.S. Patent No. 3,617,033 (Ichikawa et al). Ichikawa shows an apparatus for continuous gas-liquid contact. The apparatus may be used, for example, in refining crude terephthalic acid by contacting a suspension thereof with molecular oxygen. The apparatus includes a vertical vessel with a tapered bottom, a pipe for supplying a liquid, an opening for feeding a gas, and an opening for withdrawing the liquid. The reaction vessel may operate at a total pressure of 5-100

atmospheres. The Examiner cited Ischikawa et al. for its use of a titanium pressure vessel. As previously discussed, the apparatus of Cody et al. is designed to operate at very low pressures and would require significant modification for operation substantially above atmospheric pressure, not just with regard to the material of the manifold.

Claims 6, 7, 9, 11, 12, 16, 26, 27, 50, and 51 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Cody et al. in view of U.S. Patent No. 6,309,608 (Zhou et al.). Zhou et al. disclose multi-vessel reaction blocks designed to facilitate the semi-automated production of libraries of chemical compounds by combinatorial and parallel synthesis techniques. Zhou et al. do not remedy the deficiencies found in the primary reference, as previously discussed.

With respect to the rejection of claim 26 over Cody et al. and Zhou et al., the Examiner refers to springs 490 as being used to bias vials upward against a flow restriction device. First, Zhou et al. do not show or suggest a flow restriction device. Figs. 18A and 18B and the corresponding description (col. 16, line 36 – col. 17, line 42) of the Zhou et al. patent disclose a three-component cover plate assembly comprising a perforated cover plate top piece 920, septum sheet 940, and perforated cover plate bottom piece 960. Perforations within the top and bottom pieces are aligned with one another and the reaction vessels. The septum sheet simply allows the reaction vessels to be accessed with a syringe while being sealed off from the atmosphere. Recessed area 958 is provided on the underside of bottom piece 960 to permit purge gas as well as other gases and vapors to flow through the space above the reaction vessels (Fig. 18B, col. 17, lines 37-42). Flow between the reaction vessels is not restricted by the septum sheet. Thus, Zhou et al. do not show or suggest a flow restriction device. Secondly, springs 490 of the Zhou et al. apparatus are used to force seal plate 400 towards the bottom surface of reaction block 100 and not for biasing vials (see, Figs. 1 and 5A-5F, and col. 13, line 66- col. 14, line 2). Glass vials are not used in the reaction block 100, because vials would make it

impossible to open the reaction wells and drain or purge the contents, which is an important feature of the Zhou et al. apparatus.

The additional references cited including U.S. Patent Nos. 5,529,756 (Brennan et al.), 6,171,555 (Cargill et al.), 6,027,694 (Boulton et al.), 6,264,891 (Heynaker et al.), 5,443,791 (Cathcart et al.), 4,180,943 (Smith et al.), and 6,250,707 (Dinter et al.), do not remedy the deficiencies of the primary references.

VI. Conclusion:

In view of the foregoing, reconsideration and allowance of claims 1-37 and 42-53 are respectfully requested. If the Examiner feels that a telephone conference would in any way expedite prosecution of the application, please do not hesitate to call the undersigned at (408) 446-8695.

Respectfully submitted,



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**VERSION WITH MARKINGS TO SHOW CHANGES MADE TO THE
APPLICATION**

IN THE SPECIFICATION:

The Abstract of the Disclosure was amended as follows:

An apparatus for use in parallel reaction of materials [is disclosed. The apparatus] includes a base having a plurality of reaction wells, each of the reaction wells having a closed lower end and open upper end for receiving reactant materials. A cover is configured for sealing engagement with the base to form a housing enclosing the plurality of reaction wells and defining a common pressure chamber in communication with the reaction wells. The apparatus further includes an inlet port in communication with the pressure chamber for supplying pressurized fluid to the chamber to pressurize the reaction wells. The housing is configured to sustain a pressure substantially above atmospheric pressure.

IN THE CLAIMS:

Claims 10 and 11 are amended as follows:

Claim 10 (amended). The apparatus of claim 1 wherein the cover is removably attached to the base [member].

Claim 11 (amended). The apparatus of claim 1 wherein external dimensions of the base [member] and cover generally correspond to standard microtiter plate dimensions for use with automation equipment designed for use with microtiter plates.